REMARKS

Claims 100-165 are pending. Claims 100-129 and 135-165 are withdrawn without prejudice or disclaimer. Claims 130 to 134 are presently presented for examination. Claims 130 and 131 are currently amended. Support for the amendments to claim 130 can be found in the claims as originally filed, at page 21, lines 4-8 and elsewhere throughout the specification. Support for the amendments to claim 131 can be found in the claims as originally filed, at page 20, lines 8-30 and elsewhere throughout the specification.

Having carefully reviewed the instant Office Action, Applicants respectfully traverse the rejection of claims 130-134.

Claim rejection under 35 U.S.C. § 112, second paragraph

Claim 131 is rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. In particular, the Examiner asserts that this claim is vague and indefinite in the recitation of the phrases "functionally equivalent" and "at least part of the function" as related to the gene product of the non modified sequence because one of ordinary skill in the art would allegedly be unable to determine the metes and bounds of the claimed subject matter.

Although Applicants maintain that unamended claim 131 is definite, solely to expedite allowance of the instant application, Applicants have amended claim 131 so as to delete the phrases "functionally equivalent" and "at least part of the function."

In view of the foregoing amendment, Applicants respectfully request that the Examiner withdrawn the rejection of claim 131 as indefinite under 35 U.S.C. § 112, second paragraph.

Claim rejections under 35 U.S.C. § 112, first paragraph

Claims 130-134 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. In particular, for each of these claims, the Examiner asserts that "the genus is highly variant because a significant number of structural

differences between genus members is permitted." The Examiner then goes on to assert that the disclosure does not describe "common attributes or characteristics that identify members of the genus, and therefore, the Applicants do not demonstrate possession of the claimed invention.

Applicants respectfully submit that independent claim 130, as well as the claims dependent thereon, are adequately described by the specification. As part of the basis for the written description rejection, the Examiner has cited the cases *Fiers v. Revel*, 25 USPQ2d 1601 (CAFC 1993), *Amgen Inc. v. Chugai Pharmaceutical Co. Lts.*, 18 USPQ23 1016 and *University of California v. Eli Lilly*, 43 USPQ2d 1398 (CAFC 1997). Applicants would like to point out that in each of those cases, the claims at issue were composition claims drawn to a newly discovered protein and/or nucleic acid encoding the protein. In *Eli Lilly*, only a single sequence had been discovered yet the claims were composition claims drawn to the genus of all possible sequences from all known organisms. In contrast to the above-mentioned cases, the presently presented claims are not drawn to compositions of newly discovered gene or protein sequences. Rather, these claims are drawn to methods of using the components of proteic killer systems in novel way. As discussed further below, this novel use has been exemplified by Applicants for many different proteic killer systems. Through these examples, it is made clear that the claimed methods can be performed using any of a number of different proteic killer systems from a wide range of organisms.

Applicants would also like to point out that the Federal Circuit has held that the written description requirement can be met by describing structural elements and disclosing a function which relates to the described structural elements. *See Enzo Biochem, Inc. v. Gen-Probe, Inc.* 63 USPQ2d 1618 (CAFC 2002); *In re Wallach* 71 USPQ2d 1939 (CAFC 2004). As discussed in the following paragraphs, Applicants have described the common function of proteic killer systems and have provided a representative number of structures corresponding to each component of these systems from a diverse groups of organisms.

Claim 130 recites a method of confining an extrachromosomal replicon to a recombinant microbial cell population by utilizing a proteic killer system. The meaning of the phrase "proteic killer system" is set forth in the specification at page 8, lines 3 to 10. In particular, the specification states that proteic killer systems consist of two components. The first component comprises a cytotoxic polypeptide and the second component comprises an antitoxin that inhibits

the cytotoxin. Proteic killer systems are a subclass of plasmid addiction systems, which are described in the review article by Zielenkiewicz and Ceglowski (enclosed herewith as Exhibit A). The Zielenkiewicz review article, which was published in 2001, describes most, if not all, of the proteic killer gene systems that were characterized at the time of filing the instant application (See Table II). By comparing Table II of the Zielenkiewicz review article with the instant specification at page 29, lines 18 to 32, it can be seen that nearly all of the known proteic killer gene systems are disclosed in the instant application.

In addition to describing most of the known proteic killer systems, Applicants have identified proteic killer systems homologous to the *E. coli* RelE/RelB system in organisms other than *E. coli*. The specification at page 38, line 26 to page 40, line 4 describes homology searching that was conducted in various organisms using RelE and RelB sequence from *E. coli*. Table 1.3 of the instant specification (page 42) lists RelE homologs identified from various Gram-negative bacteria, Gram-positive bacteria and Archaebacteria. Similarly, Table 1.4 (page 43) lists the RelB homologs for each of the organisms described in Table 1.3. An alignment of the identified RelE sequences and the identified RelB sequences is displayed in Table 1.5 (page 44) and Table 1.6 (page 45), respectively. It will be appreciated, that an identical approach can be used to identify homologs, if any, to any of the other known proteic killer systems.

Thus, in summary, the specification shows that Applicants have described nearly all of the proteic killer systems known at the time of filing the instant application. Furthermore, Applicants have described a method of identifying homologs of any proteic killer system from any organism. Applicants have used this method to identify homologs of the *E. coli* RelE/RelB system in numerous species representatively distributed across a wide range of microbes. Applicants have further verified the functional activity of several of these homologs (see Examples 4-16).

In view of the foregoing remarks, Applicants respectfully request that the Examiner withdraw the rejection of claims 130-134 under 35 U.S.C. § 112, first paragraph.

Claim rejections under 35 U.S.C. § 102(b)

Claims 130-134 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Tsuchimoto et al. In particular, the Examiner asserts that Tsuchimoto et al. disclose vectors

containing the genes for PemK and PemI. The Examiner goes on to assert that Tsuchimoto et al. also disclose transforming the vectors into microbial cells and then cultivating the cells such that cells containing both PemK and PemI survive but cells containing only PemK do not.

Applicants respectfully submit that unamended, independent claim 130, as well as the claims dependent thereon, are fully patentable in view of Tsuchimoto et al. However, solely to achieve speedy allowance of the instant claims, independent claim 130 has been amended to recite that the chromosome of the cell comprises the cytotoxin polypeptide of the proteic killer gene system. Tsuchimoto et al. does not disclose methods wherein the cytotoxin polypeptide is included in the chromosome of the cell. As such, for at least this reason, Tsuchimoto does not disclose all of the elements of claims 130-134.

In view of the foregoing amendment are remarks, Applicants respectfully request that the Examiner withdraw the rejection of claims 130-134 under 35 U.S.C. § 102(b).

CONCLUSION

Applicants believe that all outstanding issues in this case have been resolved and that the present claims are in condition for allowance. Nevertheless, if any undeveloped issues remain or if any issues require clarification, the Examiner is invited to contact the undersigned at the telephone number provided below in order to expedite the resolution of such issues.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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